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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/621,784	07/16/2003	Alison M. Bendele	A-398G	1663

21069 7590 10/01/2008

AMGEN INC.
MAIL STOP 28-2-C
ONE AMGEN CENTER DRIVE
THOUSAND OAKS, CA 91320-1799

EXAMINER	
BORGEEST, CHRISTINA M	

ART UNIT	PAPER NUMBER
1649	

MAIL DATE	DELIVERY MODE
10/01/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/621,784	BENDELE ET AL.	
	Examiner	Art Unit	
	Christina Borgeest	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 June 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *27-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *27-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on *16 July 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/6/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of species IL1-RA in the reply filed on 16 November 2007 is acknowledged. Claims 27-31 are under examination.

Claim Objections

Claims 29 and 31 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 29 recites a method for treating an inflammatory condition resulting from cartilage damage and claim 31 is drawn to a method for treating ocular disease, neither of which further limits claim 27, which is drawn to a method for treating neurological disorders. Because claims 29 and 31 do not limit claim 27, they are being interpreted as independent claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claim 29 is rejected under 35 U.S.C. 102(b) as being anticipated by Lebsack et al. (A dose and regimen ranging study of IL-1 receptor antagonist or IL1-RA in patients with rheumatoid arthritis. Arthritis Rhem. 36: S39 (abstract)). Claim 29 is drawn to the treatment of patients suffering from an inflammatory condition resulting from cartilage damage with IL1-RA via subcutaneous administration. Lebsack et al. teach subcutaneous administration of IL1-RA to patients suffering from rheumatoid arthritis, an inflammatory condition that is associated with cartilage damage, thus claim 29 cannot be distinguished over the prior art.

Claim 31 is rejected under 35 U.S.C. 102(b) as being anticipated by Patel et al. (U.S. Patent No. 5,340,572, issued 23 August 1994). Claim 31 is drawn to a method of administering IL1-RA topically for treating an ocular disease. Patel et al. teach topical ophthalmic delivery of a gel suspension that contains anti-inflammatory agents selected from the group consisting of IL1-RA (see, for example, abstract, claim 13), thus claim 31 cannot be distinguished over the prior art.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000.

Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 27-30 are rejected under 35 U.S.C. 102(e) as being anticipated by anticipated by Collins et al., (U.S. Patent No.: 6,096,728, which although filed on 7 February 1997, claims benefit to U.S. Provisional application, 60/011,419, filed 9 February 1996).

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

The '728 patent teaches administration of IL1-RA to humans (see, for instance, column 4, lines 31-37) for the treatment of inflammatory conditions, including Alzheimer's disease, Parkinson's disease, ALS, trauma, rheumatoid arthritis, ischemic injury, stroke and cartilage damage, among others (see, for instance, column 1 lines 38-67 through column 2, lines 1-7). Methods of administration include may be administered via topical, enteral or parenteral administration including, without limitation, intravenous, intramuscular, intraarterial, intrathecal, intracapsular, intraorbital, intracardiac, intradermal, intraperitoneal, transtracheal, subcutaneous, subcuticular, intra-articular, subcapsular, subarachnoid, intraspinal, intraventricular and intrasternal injection and infusion, among others (see column 26, lines 62-67 through

column 27, lines 1-3). It is noted that claim 27 requires that the dose be administered intralesionally or perilesionally, and since perilesionally means "around the lesion", the term is broad and a can be reasonably interpreted as being encompassed by intraspinal or subarachnoid, since both of these are around neuronal tissue and thus the lesions can occur near them. Finally, the '728 patent contains the nucleic acid sequence of IL1-RA, which is identical to that (SEQ ID NO: 1) which is found in the instant application.

The '728 patent claims benefit to U.S. Provisional application, 60/011,419, which teaches administration of IL1-RA (see, for instance, p. 6, line 24) to humans (see, for instance, p. 4, line 29; p. 12, line 34) for the treatment of inflammatory conditions, including Alzheimer's disease, Parkinson's disease, ALS, trauma, rheumatoid arthritis, ischemic injury, stroke and cartilage damage, among others (see, for instance p. 13, lines 15-26).

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RESULT 1
US-08-798-414-1
; Sequence 1, Application US/08798414
; Patent No. 6096728
;  GENERAL INFORMATION:
;    APPLICANT:  COLLINS, David S.
;    APPLICANT:  BEVILACQUA, Michael P.
;    TITLE OF INVENTION:  COMPOSITION AND METHOD FOR TREATING
;    TITLE OF INVENTION:  INFLAMMATORY DISEASES
;    NUMBER OF SEQUENCES:  2
;    CORRESPONDENCE ADDRESS:
;      ADDRESSEE:  AMGEN INC.
;      STREET:  1840 De Havilland Drive
;      CITY:  Thousand Oaks
;      STATE:  California
;      COUNTRY:  US
;      ZIP:  91320-1789
;    COMPUTER READABLE FORM:
;      MEDIUM TYPE:  Floppy disk
;      COMPUTER:  IBM PC compatible
;      OPERATING SYSTEM:  PC-DOS/MS-DOS
;      SOFTWARE:  PatentIn Release #1.0, Version #1.30
;    CURRENT APPLICATION DATA:
;      APPLICATION NUMBER:  US/08/798,414
;      FILING DATE:  07-FEB-1997
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;      CLASSIFICATION:  514
;    PRIOR APPLICATION DATA:
;      APPLICATION NUMBER:  US 60/011,419
;      FILING DATE:  09-FEB-1996
;    PRIOR APPLICATION DATA:
;      APPLICATION NUMBER:  US 60/032,789
;      FILING DATE:  06-DEC-1996
;    PRIOR APPLICATION DATA:
;      APPLICATION NUMBER:  US (Atty Dkt# A-365B-P)
;      FILING DATE:  23-JAN-1997
;    ATTORNEY/AGENT INFORMATION:
;      NAME:  ZINDRICK, Thomas D.
;      REGISTRATION NUMBER:  32,185
;      REFERENCE/DOCKET NUMBER:  A-365C
;  INFORMATION FOR SEQ ID NO:  1:
;    SEQUENCE CHARACTERISTICS:
;      LENGTH:  462 base pairs
;      TYPE:  nucleic acid
;      STRANDEDNESS:  single
;      TOPOLOGY:  linear
;    MOLECULE TYPE:  cDNA
;    FEATURE:
;      NAME/KEY:  CDS
;      LOCATION:  1..462
;    FEATURE:
;      NAME/KEY:  misc_feature
;      LOCATION:  1..3
;      OTHER INFORMATION:  /note= "Initial methionine is
;      OTHER INFORMATION:  optional."
US-08-798-414-1

  Query Match             100.0%;  Score 459;  DB 3;  Length 462;
  Best Local Similarity   100.0%;  Pred. No. 1.8e-134;
  Matches  459;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps
c 0;

Qy          4 CGACCCTCTGGGAGAAAATCCAGCAAGATGCAAGCCTTCAGAATCTGGGATGTTAACCAG 63
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          4 CGACCCTCTGGGAGAAAATCCAGCAAGATGCAAGCCTTCAGAATCTGGGATGTTAACCAG 63

Qy         64 AAGACCTTCTATCTGAGGAACAACCAACTAGTTGCTGGATACTTGCAAGGACCAAATGTC 123
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         64 AAGACCTTCTATCTGAGGAACAACCAACTAGTTGCTGGATACTTGCAAGGACCAAATGTC 123

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              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Qy        184 CATGGAGGGAAGATGTGCCTGTCCTGTGTCAAGTCTGGTGATGAGACCAGACTCCAGCTG 243
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Db        244 GAGGCAGTTAACATCACTGACCTGAGCGAGAACAGAAAGCAGGACAAGCGCTTCGCCTTC 303

Qy        304 ATCCGCTCAGACAGTGGCCCCACCACCAGTTTTGAGTCTGCCGCCTGCCCCGGTTGGTTC 363
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Qy        364 CTCTGCACAGCGATGGAAGCTGACCAGCCCGTCAGCCTCACCAATATGCCTGACGAAGGC 423
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        364 CTCTGCACAGCGATGGAAGCTGACCAGCCCGTCAGCCTCACCAATATGCCTGACGAAGGC 423

Qy        424 GTCATGGTCACCAAATTCTACTTCCAGGAGGACGAGTAG 462
              |||||||||||||||||||||||||||||||||||||||
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Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 27 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Relton and Rothwell (Brain Research Bulletin, 1992; 29: 243-246).

The first factor that must be considered when determining obviousness is to determine the scope and contents of the prior art. Relton and Rothwell (hereafter

"Relton") teach administration of IL-1 receptor antagonist protein, or IL1-RA, to rats induced with cerebral ischemia (see p. 243, right column through p. 244, left column) via intracerebral injection (p. 245, left column, under "Discussion") with the result that low doses of IL1-RA inhibited ischemic damage in the brain (see p. 246, right column, last paragraph).

The second factor that must be considered is to ascertain the differences between the prior art and the instant claims. Relton teaches all of the limitations of the claims with the exception that the claims recite treatment of a human, whereas Relton teaches administration in the rat. The claims would have been obvious because a person of ordinary skill in the art (POSITA) has good reason to pursue the known options within his or her technical grasp, and in the instant case, the POSITA would recognize that the rat model of cerebral ischemia is a good model for ischemia or stroke in humans. Note the teachings of Relton at p. 245, left column under "Discussion": "[middle] cerebral artery occlusion is widely recognized as a reliable and clinically relevant experimental procedure for introduction of cerebral ischemia," thus also providing evidence that this would be well within the skill of the POSITA to recognize the relevance of this experimental model.

Finally, one must consider objective evidence present in the application indicating obviousness or nonobviousness. In the instant case, the experiments described in the specification were performed on rats, thus this is not in conflict with the teachings of Relton. In addition, there is no evidence of unexpected results on humans disclosed in the specification. Therefore, it would have been obvious to the POSITA at

the time of the invention to modify the teachings of Relton by administering IL1-RA to a human because for the reasons outlined in the preceding paragraph, the POSITA would recognize that the rat model of cerebral ischemia is a good model for ischemia or stroke in humans. In addition, it is generally known in the medical arts that rats are used as models for testing pharmaceuticals intended for humans. Thus for the reasons outlined above, claims 27 and 28 are obvious in view of Relton.

Claim 30 is rejected under 35 U.S.C. 103(a) as being unpatentable over Relton and Rothwell (cited above, hereafter "Relton") as applied to claims 27 and 28 above, and further in view of Lebsack et al. (cited above).

The discussion above regarding the determination of the scope and contents of the prior art and how Relton meets the limitations of administration of IL1-RA for the purpose of treating ischemia and how this treatment would be obvious to try in humans is hereby incorporated into this rejection.

The second factor that must be considered is to ascertain the differences between the prior art and the instant claims. Relton does not teach subcutaneous administration. Nevertheless, the claim would have been obvious because the POSITA has good reason to pursue the known options within his or her technical grasp, and in the instant case, the POSITA would recognize that subcutaneous administration, i.e., administration under the skin, would be a medically relevant alternative to intra- or peri-lesional administration, not least of all because of the ease of which subcutaneous administration can be performed. In addition, Lebsack et al. teach subcutaneous

administration to humans with mostly mild injection site reactions reported, that resulted in only a 5% discontinuation rate in the study, thus also providing evidence that this would be well within the skill of the POSITA to recognize the relevance of this injection method.

Finally, one must consider objective evidence present in the application indicating obviousness or nonobviousness. In the instant case, there is no evidence of unexpected results as a result of subcutaneous administration of IL1-RA disclosed in the specification. Therefore, it would have been obvious for the POSITA to modify the teachings of Relton by administering the IL1-RA subcutaneously, as taught in Lebsack et al., because the POSITA would recognize that subcutaneous administration, i.e., administration under the skin, would be a medically relevant alternative to intra- or peri-lesional administration. Thus for the reasons outlined above, claim 29 is also obvious in view of Relton and Lebsack et al.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christina Borgeest whose telephone number is (571)272-4482. The examiner can normally be reached on 8:00am - 2:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on 571-272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Christina Borgeest, Ph.D.

/Elizabeth C. Kemmerer/
Primary Examiner, Art Unit 1646